UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,119	04/12/2004	Walter Muller	512100-2034	3517

20999 7590 06/02/2010
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
06/02/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,119	MULLER, WALTER	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicant's amendment filed 02/25/2010.

Claims 1-20 previously prosecuted, and claims 21-23 are currently added.

Claims 1-23 are pending and included in the prosecution.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32-55 of copending Application No. 10/835,997 in view of Robbins (US 6,239,180). The subject matter claimed in the instant application is fully disclosed in the referenced copending applications and would be covered by any patent granted on the copending applications since the referenced copending applications and the instant application are subject matter as follows: transdermal patch comprising self adhesive polysiloxane matrix containing microreservoirs comprising an active agent in an amphiphilic solvent and method of making the transdermal patch including the steps of dissolving the active agent in amphiphilic solvent, mixing the drug solution with polysiloxane solution to form dispersion, coating the dispersion onto protective liner, removing the solvent of the polysiloxane to form matrix, laminating a backing layer to the dried matrix.

However, the present claims are different from the copending claims because the copending claims not drawn to capsaicin while the present claims recite capsaicin.

Robbins teaches transdermal patch to deliver capsaicin or capsaicin analog that are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time (abstract; col.2, lines 26-30; col.3, lines 62-65; col.4, lines 12-13).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal patch comprising self adhesive polysiloxane matrix containing microreservoirs comprising an active agent dissolved in an amphiphilic solvent as claimed by the copending application '997, and deliver capsaicin taught by Robbins in the microreservoirs claimed by the copending

application. One would have been motivated to do so because Robbins teaches that capsaicin or capsaicin analog when delivered in transdermal patch are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time. One would reasonably expect formulating transdermal patch comprising self adhesive polysiloxane matrix containing microreservoirs comprising capsaicin or its analogs in an amphiphilic solvent to treat neuropathic pain effectively for prolonged period of time.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

3. Applicant's arguments filed 02/25/2010 have been fully considered but they are not persuasive.

Applicant argues that while there are certain similarities between the analysis for an obviousness rejection and an obviousness-type double patenting (ODP) rejection, the rejections are not the same, i.e. the analysis for an ODP rejection is limited to a comparison of the respective claims and does not allow for the use of secondary references except for explanatory purposes. However, Robbins is being used to address a missing element of the applicants' claim. Therefore, the use of the Robbins is prima facie evidence that a basis for ODP does not exist. Moreover, even if Robbins had been an appropriate reference for use, Robbins was specifically directed to capsaicin and capsaicin analogs; it is not instructive of selecting capsaicin and capsaicin analogs from a generic teaching of a therapeutic compound or was predictive

of the fact that the permeation rate of capsaicin and capsaicin analogs could be doubled by the use of microreservoirs of amphiphilic solvent in the matrix of the topical patch.

In response to this argument, it is argued that the present claims 1-23 are obvious over the claims 32-55 currently pending in copending application US '997 that has earlier filing date and not reciting any drugs. Robbins is used as an explanatory reference showing capsaicin can be administered transdermally. The copending application claims transdermal delivery system having the same structure and composition as the instantly claimed. Therefore, at the time of the invention the structure of the claimed transdermal device was claimed by US '977. Robbins teaches capsaicin and its analogs when delivered in transdermal patch are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time. Therefore, combination of the claims pending in US '997 that has earlier filing date and the teaching of Robbins would have resulted in the present claims 1-23.

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. Applicant has not indicated check and review of the application, nor any correction has been made to the specification. Therefore objection to the specification has been maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description rejection. The present claims recite "capsaicin analog". The specification failed to describe any "capsaicin analogs" to satisfy the written description requirements. Because the instant specification does not provide written description of what structures are contemplated for such "capsaicin analog", this phrase lacks adequate written description. Regarding the requirement for adequate written description of chemical entities, Applicants' attention is directed to MPEP § 2163. In particular, *Regents of the University of California v. Eli Lilly & Co.,* 119 F. 3d 1559, 1568 (Fed. Cir. 1997), cert denied, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish list or plan for obtaining the claimed chemical invention." *Eli Lilly,* 119 F. 3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the

U.S.C. 112.1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including inter alia, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F. 3d 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Eli Lilly and Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.,* 249 Supp. 2d 216,225 (W.D.N.Y. 2003).

Applicant has failed to provide any written description for "capsaicin analog" in the instant specification. As such, it is not apparent that Applicant was actually in possession of, and intended to use, within the context of the present invention, any capsaicin analogue at the time the present invention was made. The specification neither provides any analogs required to practice the inventions, nor "inform the public" during the life of the patent of the limits of the monopoly asserted.

Response to Arguments

8. Applicant's arguments filed 02/25/2010 have been fully considered but they are not persuasive.

Applicant argues that the Office Action cited U.S. Patent 6,239,180 ("Robbins '180") in the obviousness and obviousness-type double patenting rejections. Robbins

'180 and Robbins (U.S. Patent 6,248,788) are both described in the applicants' background section of the specification. Robbins '180 not only refers to "capsaicin analogs" throughout their specification, but it is also part of their claims (see e.g. claims 1 and 3). As such, one of ordinary skill in the capsaicin arts is apprised of the meaning and scope of the term capsaicin analog and would have presumed that the applicants and Robbins had possession of the concept of capsaicin analog absent any evidence to the contrary. Lastly, the applicants note that maintaining this rejection is an implicit rejection of the allowed claims of Robbins ' 180. However, each claim of a patent is presumed to be valid. See 35 U.S.C. 282. As such, maintaining this rejection is casting aspersions on a previously issued U.S. patent which is explicitly not permitted.

In response to this argument, the examiner respectfully disagrees because applicant did not incorporate by reference Robbins' patents. Further, Robbins' patent do not describe what are the "capsaicin analogs"?. Applicant is not in possession of "capsaicin analogs" as of the filing date of the present application.

Further, the examiner is not oriented with the prosecution history of Robbins' applications in order to decide if enough evidence to support "analog" has been provided during prosecution of Robbins' patent applications.

Applicant should provide response about the current rejection instead arguing what another examiner's arguments and decisions in the previous application. Every application is examined on its criteria following the guidelines for patent examination. Further, the examiner cannot comment on the prosecution history of another patent.

Regarding MPEP 1701, it is irrelevant to this issue. MPEP 1701 [R-3], it is directed to **"Office Personnel Not To Express Opinion on Validity, Patentability, or Enforceability of Patent"**

This section stated:

"Every patent is presumed to be valid. 35 U.S.C. 282, first sentence. Public policy demands that every employee of the United States Patent and Trademark Office (USPTO) refuse to express to any person any opinion as to the validity or invalidity of, or the patentability or unpatentability of any claim in any U.S. patent, except to the extent necessary to carry out

(A) an examination of a reissue application of the patent,

(B) a reexamination proceeding to reexamine the patent, or

(C) an interference involving the patent. The question of validity or invalidity is otherwise exclusively a matter to be determined by a court. Likewise, the question of enforceability or unenforceability is exclusively a matter to be determined by a court. Members of the patent examining corps are cautioned to be especially wary of any inquiry from any person outside the USPTO, including an employee of another U.S. Government agency, the answer to which might indicate that a particular patent should not have issued. No USPTO employee may pursue a bounty offered by a private sector source for identifying prior art. The acceptance of payments from outside sources for prior art search activities may subject the employee to administrative disciplinary action. When a field of search for an invention is requested, examiners should routinely inquire whether the invention has been patented in the United States. If the invention has been patented, no field of search should be suggested. Employees of the USPTO, particularly patent examiners who examined an application which matured into a patent or a reissued patent or who conducted a reexamination proceeding, should not discuss or answer inquiries from any person outside the USPTO as to whether or not a certain reference or other particular evidence was considered during the examination or proceeding and whether or not a claim would have been allowed over that reference or other evidence had it been considered during the examination or proceeding. Likewise, employees are cautioned against answering any inquiry concerning any entry in the patent or reexamination file, including the extent of the field of search and any entry relating thereto. The record of the file of a patent or reexamination proceeding must speak for itself. Practitioners shall not make improper inquiries of members of the patent examining corps. Inquiries from members of the public relating to the matters discussed above must of necessity be refused and such refusal should not be considered discourteous or an expression of opinion as to validity, patentability or enforceability. The definitions set forth in 37 CFR 104.1 and the exceptions in 37 CFR 104.21 are applicable to this section."

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller (WO 01/01967, translation currently provided) in view of Robbins (US 6,239,180) and Schacht et al. (US 2005/0079206).

Applicant Claims

Applicant claims a topical patch comprising a therapeutic compound-impermeable backing layer, a self-adhesive amine-resistant polysiloxane matrix containing at least 1% by weight, of the therapeutic compound wherein the polysiloxane matrix is a mixture of a polysiloxane of medium tack and a polysiloxane of high tack and the therapeutic compound is capsaicin or a capsaicin analog or mixture thereof, and a protective film to be removed before use, in which

a) the matrix contains liquid microreservoir droplets comprising an amphiphilic solvent, in which the therapeutic compound is dissolved, and

b) the concentration of the therapeutic compound in the microreservoir droplets is between 20 and 90% by weight of the saturation concentration wherein the amphiphilic

solvent is a butanediol, 1,3-butanediol, dipropylene glycol, tetrahydrofurfuryl alcohol, diethylene glycol dimethyl ether, diethylene glycol monoethyl ether, diethylene glycol monobutyl ether, propylene glycol, dipropylene glycol, carboxylic acid esters of tri- and diethylene glycol, polyethoxylated fatty alcohols of 6 - 18 C atoms or 2,2-dimethyl-4-hydroxymethyl- 1,3-dioxolane, or mixtures of these solvents. Claim 20 further recite conventional method of making the device.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

Muller teaches transdermal therapeutic system on the basis of polysiloxane which contains microreservoirs filled with an active agent and amphiphilic solvent (abstract). The transdermal therapeutic system comprises backing layer impermeable to the active agent, matrix containing microreservoirs containing active agent dispersed in amine resistant polysiloxane polymer, and removable protective liner (page 2, page 4). The amphiphilic solvents include 1,3-butaindiol, dipropylene glycol, tetrahydrofurfuryl alcohol, diethylene glycol monoethyl ether (page 3). Examples showed that the concentration of the therapeutic agent in the amphiphilic solvent is from 1-30%, and forming at least 1% of the total matrix. The microreservoirs further comprise viscosity enhancer agents including ethyl cellulose, hydroxypropyl cellulose, high molecular weight polyacrylic acid (page 4). The polysiloxane matrix comprises tackyfying agent such as silicone oil (page 5). The backing layer is made of polyester or ethylene-vinyl-acetate copolymer (page 5). The therapeutic agents include analgesics (page 5). The

reference teaches method for making the device comprising the steps of dissolving the active agent in the amphiphilic solvent and mix the solution with polysiloxane solution, forming dispersion of the active agent, coating the dispersion on a abhesively treated film, removing the solvent to form a matrix, and laminating a backing layer onto the dried matrix (page 3).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Although Muller teaches suitability of the disclosed transdermal system to deliver analgesics agent, however, the reference does not explicitly teach capsaicin as analgesic active agent dissolved in the microreservoirs.

Although Muller teaches that polysiloxane suitable as matrix for microreservoirs comprising amphiphilic solvent and active agent, however, the reference does not explicitly teach mixture of medium tack polysiloxane and high tack polysiloxane.

Robbins teaches transdermal patch to deliver capsaicin or capsaicin analog that are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time (abstract; col.2, lines 26-30; col.3, lines 62-65; col.4, lines 12-13).

Schacht teaches transdermal device comprising microreservoirs containing drug in a self adhesive matrix, wherein the matrix is silicone adhesive made of mixture of high tack polysiloxane (BIO-PSA 4301) and medium tack polysiloxane (BIO-PSA 4201) that is advantageous in providing optimum balance between good adhesion and little cold flux (abstract; paragraphs: 0054-0058).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

Therefore, the prior art at the time of the invention recognized microreservoirs containing therapeutic agent dissolved in amphiphilic solvent within polysiloxane matrix as taught by Muller. The art further recognized capsaicin can be delivered transdermally to treat neuropathic pain as taught by Robbins. Mixture of medium tack polysiloxane and high tack polysiloxane was also known as advantageous adhesive for transdermal devices at the time of the invention as taught by Schacht.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising a polysiloxane polymer matrix comprising microreservoirs containing analgesic agent dissolved in amphiphilic solvent as taught by Muller, and replace the analgesic agent with capsaicin or capsaicin analog taught by Robbins. One would have been motivated to do so because Robbins teaches that capsaicin or capsaicin analog when delivered in transdermal patch are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time. One would reasonably expect formulating transdermal patch comprising polysiloxane matrix containing microreservoirs comprising capsaicin or its analogs dissolved in an amphiphilic solvent to treat neuropathic pain effectively for prolonged period of time.

Additionally, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal patch comprising polysiloxane matrix

containing microreservoirs comprising capsaicin or its analogs dissolved in an amphiphilic solvent as taught by the combined teaching of Muller and Robbins, and replace the polysiloxane matrix with matrix comprising mixture of high tack polysiloxane and medium tack polysiloxane as taught by Schacht. One would have been motivated to do so because Schscht teaches that such a mixture is advantageous when used in transdermal patches because it provides optimum balance between good adhesion and little cold flux. One would reasonably expect formulating transdermal device comprising microreservoirs comprising capsaicin or its analogs dissolved in amphiphilic solvent and the microreservoirs are dispersed in matrix made of mixture of high tack polysiloxane and medium tack polysiloxane wherein the matrix has optimum balance between good adhesion and little cold flux.

The references do not teach the exact concentration of the active agent in the microreservoirs or concentration of microreservoirs in the matrix as claimed by claims 3, 10, 11, 13, 14, the coating weight of the drug containing adhesive on the backing layer as claimed by claims 13 and 14, or the thickness of the backing layer as claimed by claim 15. However, the concentration of the active agent and microreservoirs, coating weight, and thickness of the backing would have been determined by one having ordinary skill in the art without undue experimentation based on the specific individual use. Such variants do not impart patentability of the claims in absence of superior and unexpected results.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

12. Applicant's arguments filed 02/2/2010 have been fully considered but they are not persuasive.

A. Allowability of species inventions over the genus invention

Applicant argues that During the 8 December 2009 interview between the Examiner and the applicants' representative (Howard C. Lee), it appeared a general agreement was reached that this application represented a "species" invention in relation to the "genus" represented by the '997 application, the present application is specifically directed toward capsaicin and capsaicin analogs instead of being generically directed to therapeutic compounds. Applicants have already received a "species" patent wherein the therapeutic compound was fentanyl (see U.S. Patent 7,390,500). As such, the applicants were confused by the nature of the rejection for this application (as well as the genus application) as the rejection appears to be revisiting old issues which have already been decided, i.e. the Examiner in the '500 patent also considered WO 01/01967 and the fentanyl claims in the '500 patent were allowed.

Again, in response to this argument, it is argued that Applicant should response about the current rejection instead arguing what another examiner's arguments and decisions in the previous application. Every application is examined on its criteria

following the guidelines for patent examination. Further, the examiner cannot comment on the prosecution history of another patent. The present invention is directed to capsaicin and its analog and the genus application '997 is directed to estradiol, bupranolol and testosterone. The issued patent is directed to transdermal device for delivering fentanyl. Therefore, each application has its own criteria. See also the argument regarding MPEP 1701, set forth in this office action. Each application stands by itself on the merit.

B. No rationale for combining WO 01/01967 with Robbins and Schacht

Applicants argue that WO 01/01967 is generic for therapeutic compounds, but Robbins does not provide the requisite teaching or suggestion to combine capsaicin or capsaicin analog into the applicants' topical patch because Robbins clearly requires an anesthetic in combination with their invention which is not a required element of the present invention. Moreover, Robbins cannot even contemplate that high concentrations of capsaicin is even possible without an anesthetic. Therefore, Robbins does not suggest the replacing of capsaicin as the therapeutic compound, but a combination of capsaicin and an anesthetic as the therapeutic compound i.e. even if one of ordinary skill in the art was limited to considering only the substitution of a single compound with another compound, such a selection would present an virtually an infinite number of possible solution to the problem of delivery of an analgesic.

In response to this argument, it is argued that the present claims' language "comprising" does not exclude the presence of anesthetic agent or any other agent,

active or inactive, even in major amounts. See *Moleculon Research Corporation v CBS, Inc.* 229 USPQ 805, *In re Baxter* 210 USPQ 795, 803. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). Further, the present claims are directed to a product, and all the elements of the product are taught by the combination of the cited prior art. Robbins clearly teaches transdermal patch comprising 7.5% capsaicin as the only pain treatment agent, and also teaches, preferably, a kit comprising two patches, the transdermal patch comprising the capsaicin and a second patch comprising anesthetic (col.2, lines 26-35). Therefore, Robbins teaches a transdermal patch comprising capsaicin by itself without anesthetic, however, preferred a kit that provide anesthetic patch along with capsaicin patch. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Therefore, no confusion of selecting capsaicin from the teachings of Robbins because Robbins does not teach infinite number of analgesics as applicant asserts.

Applicant further argues that Schacht is directed toward addressing the difficulties associated with rotigotine which is structurally and functionally different than capsaicin. The teaching of Schacht attempted to address the problem associated with rotigotine and suggested use of crystallization inhibitors which is not a problem in the

present invention because the capsaicin is dissolved in the microreservoir. As such, one of ordinary skill in the art would not have been directed to taking the isolated element of a mixture of high tack polysiloxane and medium tack polysiloxane as taught by Schacht for use of a rotigotine delivery system into a topical patch for capsaicin or analog.

In response to this argument, it is argued that Schacht' reference is relied upon for its generic teaching of different types of pressure sensitive adhesive that are known in the art. Schacht teaches materials suitable for self adhesive matrix for transdermal devices comprising microreservoirs. The references teaches silicone adhesive known in the art including those made of mixture of high tack polysiloxane (BIO-PSA 4301) and medium tack polysiloxane (BIO-PSA 4201) and describe them as being advantageous in providing optimum balance between good adhesion and little cold flux, therefore have nothing to do with the drug delivered. The properties of the mixture of polysiloxane adhesives having different tacks as taught by Schacht is not related to any specific drug, rather properties of the adhesive itself and therefore preferred by Schacht. For this advantage, Schacht used this mixture of polysiloxane adhesives having different tack to deliver rotigotine. Schacht did not describe the mixture of polysiloxane adhesives as specific for rotigotine. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from

knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

C. Combination of WO 01/01967, Robbins and Schacht does not suggest that capsaicin/microreservoir system would have a permeation rate which is double that of a system without mieroreservoirs

Applicant argues that the applicants have shown that a topical patch of the invention has a permeation rate which is twice that of a topical patch which does not have a microreservoir system. Neither Robbins not Schacht would have predicted this unexpected permeation rate for capsaicin in the claimed topical patch. Likewise, whereas WO 01/01967 is generic for therapeutic compounds and could encompass capsaicin, there is no suggestion that capsaicin should be selected as a preferred analgesic because of the unexpected permeation rates as has been shown by applicants.

In response to this argument, it is argued that **a prima facie case of obviousness has been established** from combination of Muller, Robbins and Schacht because all elements of the claimed invention as a whole are taught by combination if the cited references. **There is motivation to combine the references** because Muller teaches transdermal therapeutic system comprising a polysiloxane polymer matrix

comprising microreservoirs containing analgesic agent dissolved in amphiphilic solvent, and the art further recognized capsaicin can be delivered transdermally to treat neuropathic pain as taught by Robbins. Mixture of medium tack polysiloxane and high tack polysiloxane was also known as advantageous adhesive for transdermal devices at the time of the invention as taught by Schacht. Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal patch to deliver analgesics from microreservoirs a drug dissolved in amphiphilic solvent and the microreservoirs are dispersed in polysiloxane matrix as taught by Muller, and replace the analgesic agent with capsaicin or capsaicin analog taught by Robbins. One would have been motivated to do so because Robbins teaches that capsaicin or capsaicin analog when delivered in transdermal patch are extremely effective therapy for treating peripheral neuropathic pain for prolonged period of time. One would have been motivated use mixture of polysiloxane adhesives of different tacks because Schacht teaches that such a mixture is advantageous when used in transdermal patches because it provides optimum balance between good adhesion and little cold flux. **A reasonable expectation of success exists**, which is formulating transdermal device comprising microreservoirs comprising capsaicin or its analogs dissolved in amphiphilic solvent and the microreservoirs are dispersed in matrix made of mixture of high tack polysiloxane and medium tack polysiloxane wherein the matrix has optimum balance between good adhesion and little cold flux.

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there

is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071,5 USPQ2d 1596 (Fed. Cir. 1988)and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." KSR Int '1 Co. v. Teleflex Inc., 127 S.Ct. 1727, 1740 (2007) (quoting Sakraida v. AG Pro, Inc., 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL. (2007).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter as a whole as defined by the claims would have been prima facie obvious within the meaning of 35 U.S.C. 103 (a).

It is noted that the permeation rate that is shown to be doubled is not claimed. the objective evidence of nonobviousness must be commensurate in scope with claims that evidence is offered to support. See in *Greenfield and DuPont* 197 USPQ 227 (CCPA 1978); *In re Boesch and Slaney* 205 USPQ 215 (CCPA 1980); and *In re Tiffin and Erdman* 170 USPQ 88 (CCP 1971).

D. Note about FDA approved product within the scope of pending claims

Although the purpose and function of the USPTO and the FDA are different, the applicants note for the record that the product QUTENZA® has been approved for sale in the U.S. and that QUTENZA® has been designated with Orphan Drug status for the treatment of neuropathic pain associated with postherpetic neuralgia.1 (see attacbanents - "Highlights of Prescribing Information" and article from Medical News Today dated 3 June 2009) Whereas a patented product is normally delayed for sale in the U.S. because of the lengthy FDA approval process, we have the highly unusual situation whereby the FDA approval for the product has been granted before the patent covering the product.

In response to this argument, it is pointed out to these sections from MPEP:

"The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety

and efficacy of drugs to marketed in the United States. **FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws.** *Scott [v. Finney]*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 [(Fed.Cir. 1994)]. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. **The Office must confine its review of patent applications to the statutory requirements of the patent law.** Other agencies of the government have been assigned the responsibility of ensuring conformance to standards established by statute for the advertisement, use, sale or distribution of drugs. The FDA pursues a two-prong test to provide approval for testing. Under that test, a sponsor must show that the investigation does not pose an unreasonable and significant risk of illness or injury and that there is an acceptable rationale for the study. As a review matter, there must be a rationale for believing that the compound could be effective. If the use reviewed by the FDA is not set forth in the specification, FDA review may not satisfy 35 U.S.C. 101. However, if the reviewed use is one set forth in the specification, Office personnel must be extremely hesitant to challenge utility. In such a situation, experts at the FDA have assessed the rationale for the drug or research study upon which an asserted utility is

based and found it satisfactory. Thus, in challenging utility, Office personnel must be able to carry their burden that there is no sound rationale for the asserted utility even though experts designated by Congress to decide the issue have come to an opposite conclusion. "FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws." *In re Brana,* 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) (citing *Scott v. Finney,* 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994))."

"Thus, while an applicant may on occasion need to provide evidence to show that an invention will work as claimed, it is improper for Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness. See *In re Sichert,* 566 F.2d 1154, 196 USPQ 209 (CCPA 1977); *In re Hartop*, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); *In re Anthony*, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969); *In re Watson*, 517 F.2d 465, 186 USPQ 11 (CCPA 1975); *In re Krimmel,* 292 F.2d 948, 130 USPQ 215 (CCPA 1961); *Ex parte Jovanovics*, 211 USPQ 907 (Bd. Pat. App. & Inter. 1981)."

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

IG